## REMARKS

Claims 1-69 are presently pending. Claims 7-20, 23, 31, 41-57, 59, 61-62, and 67 have been canceled without prejudice. Claims 1, 4, 6, 21-22, 24-25, 29-30, 34, 36-40, 58, 60, 63-66, and 69 have been amended to further clarify the claimed invention and to provide uniformity throughout the claims. New claims 70-88 are presented herein.

Applicants respectfully assert that the amendments presented herein further clarify the invention, and do not introduce any new matter. In addition, a number of claims have been cancelled to reduce the number of issues.

Claims 1-69 have been subjected to restriction as pertaining to distinct inventions. The claims have been restricted to one of the following groups:

I. Claims 1-3, and 23 allegedly drawn to a double stranded RNA complex comprising a first portion capable of hybridizing under physiological conditions to an mRNA, and further comprising a second portion capable of hybridizing to the first, wherein the two portions are located on separate molecules, classified in class 536, subclass 24.5;

II. Claims 4-8, 12, 13, 15, 16, 18, 21-22, 24-33, 61, 62, 64-66, and 68 allegedly drawn to a linear double-stranded RNA complex comprising a first portion capable of hybridizing under physiological conditions to an mRNA, a second portion capable of hybridizing to the first, and a third portion of RNA that comprises a ribozyme and a target sequence which is cleaved by the ribozyme, classified in class 536, subclass 24.5;

III. Claims 4-11, 15, 22, and 68 allegedly drawn to a linear double stranded RNA complex comprising a first portion capable of hybridizing under physiological conditions to an mRNA, a second portion capable of hybridizing to the first, and a third portion of RNA encoding the protein Tat, classified in class 536, subclass 24.5;

IV. Claims 4-7, 19, 20, 68, and 69 allegedly drawn to a double stranded RNA complex that comprises a first portion that hybridizes to an mRNA, a second portion capable of hybridizing to the first and further comprises a polyadenylation signal and a ribozyme capable of cleaving said polyadenylation signal, classified in class 536, subclass 24.5;

V. Claims 4-8, 15, 17, 22, and 68 allegedly drawn to a double-stranded RNA complex comprising a first portion that hybridizes to an mRNA, and a second portion capable

of hybridizing to the first, wherein the second portion comprises a polyadenylation signal, classified in class 536, subclass 24.5;

VI. Claims 4-8, 14, 15, 22, and 68 allegedly drawn to a double-stranded RNA complex comprising a first portion that hybridizes to an mRNA, and a second portion capable of hybridizing to the first, wherein the second portion comprises an intron or a linker, classified in class 536, subclass 24.5;

VII. Claims 34-58, 60, and 63 drawn to methods of inhibiting protein expression using a double stranded RNA comprising a first and second portion which comprises a polyadenylation signal and a hammerhead ribozyme, classified in class 514, subclass 44.

VIII. Claims 59 and 67, drawn to a method of identifying the function of a gene in a cell using a double stranded RNA molecule, classified in class 435, subclass 6.

Applicants respectfully traverse the requirement. The requirement does not provide a reasonable way of dividing the subject matter.

For example, there are two lines of claims directed to related types of RNAs:

Claim 1 as currently amended is directed to double-stranded RNA complexes comprising:

(a) a first portion comprising a first ribonucleic acid sequence that hybridizes under physiological conditions to at least a portion of an mRNA molecule;

(b) a second portion comprising a second ribonucleic acid sequence, at least a portion of which is capable of hybridizing under physiological conditions to the first portion; and

(c) an additional ribonucleic acid sequence that enhances the ability of dsRNA to alter expression of the gene encoding the mRNA molecule.

Claim 4 is directed to linear RNA molecules capable of forming the double-stranded RNA complex of claim 1.

There is no group in the current restriction requirement which rationally encompasses the limitations of either of these claims. Further, Applicants submit that there is no group in which claim 1 and 4 both appear, although there would not be any additional substantial burden on the Office to search these two claims together. Applicants respectfully assert that claims 1 and 4 should be rejoined into a single group for the purposes of examination. The

major difference between the two claims is that claim 1 permits the RNA components to be on different molecules, while claim 4 requires that the RNA be a linear molecule encompassing the same RNA components. The second RNA portion in each claim hybridizes to the first portion, but in claim 4 it must form part of a hairpin structure, in that the molecule is a linear one. In both claim 1 and 4, the third portion enhances the ability of dsRNA to alter expression of the gene encoding the mRNA molecule. Applicants respectfully submit that a proper search of claim 1 would certainly uncover references related to claim 4, for example, and thus there would be no additional burden on the Office.

Likewise, independent claim 58 as currently amended is directed to methods for modulating expression of a specific nucleic acid sequence in a first cell comprising exposing the first cell to culture medium which has been used to maintain a second cell in culture; said second cell containing nucleic acid sequence encoding a sense strand for the specific nucleic acid and an antisense strand thereto; wherein said first cell is mammalian.

No group to which the claims are being required to be restricted rationally encompasses this claim. It is only mentioned in Group VII, a group which requires the presence of polyadenylation signal and a hammerhead ribozyme - neither of which appear in the claim. Further, this group is also populated with claim 34 and claims dependent thereon. Claim 34 is directed to methods of inhibiting protein expression in a cell through the introduction of the RNAs of claims 1 and 4, or DNAs or vectors encoding or comprising them, into the cell. These methods encompass different limitations from those recited in claim 58 and claims dependent thereon, but neither set of claims requires the polyadenylation signal and hammerhead ribozyme as is required in Group VII of the instant requirement.

Other examples of claims, for example dependent claims, that are not adequately covered under any of the groups need not be recited at length. However, in view of the foregoing, Applicants respectfully request further reconsideration of the reissued restriction requirement. Applicants note that the amendments and cancellations made herein will facilitate more satisfactory examination of the claims, and division if necessary.

To be fully responsive to the requirement, Applicants provisionally elect Group I for further prosecution in the current application. Applicants reserve the right to prosecute claims directed to any non-elected inventions, deemed herein as distinct, in one or more continuing or divisional applications.

**Conclusion:**

All claims are in condition for examination and subsequent allowance. The examiner is invited to contact the Applicants' representative to further discuss the claims or the restriction requirement. The Applicants' representative is Dr. Myra McCormack, Reg. No.: 36,602. She can be reached during normal business hours at 732-524-6932.

Respectfully submitted,

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